NavMed 369

UNITED STATES NAVY

MEDICAL NEWS LETTER

Editor - Captain L. B. Marshall, MC, USN

Vol. 18 Friday, 19 October 1951 No. 8

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Circular Letters:

Epidemic Hemorrhagic Fever (Songo Fever)

Since their presence in Northern Manchuria in 1939, the Japanese have experienced outbreaks of this disease, otherwise known as Songo, Sun-wu, Kokka, Korin or Nidoko fever. Epidemic hemorrhagic fever (EHF) is an acute infectious disease characterized by an abrupt onset with high fever, headache, myalgia, hemorrhagic diathesis, albuminuria and a leukemoid leukocytosis.

The Japanese report the specific causative agent to be a filtrable virus. They have been able to induce an apparently identical disease in monkeys by injection with ground, saline-suspended mites (Laelaps jettmari Vitzthum) recovered from the supposed host reservoir, Apodemus agrarius (old world field mouse) and have been able to transmit this infection via blood to a second monkey. The supposed reservoir host animal does not suffer apparent disease, although its viscera become infectious after experimental inoculation.

Epidemiology. The Japanese literature states that the infection is acquired from bite of the mite, that no bite marks can be observed and that the mites show no engorgement. They believe that the virus passes from the salivary gland of the mite into the puncture during the biting process. Ibuki believes that the body louse, P. humanus corporis, may also be a vector. Peak incidence, May-June and October-November, coincides with greatest reproduction of the mites. EHF is especially prevalent in areas along river banks and in swampy marshlands where the grass grows high, terrain apparently affording ideal habitat for Apodemus agrarius. Troops were more commonly affected when in bivouac than in more permanent camps. Cavalry troops receiving hay for their horses from certain areas seemed more affected than others. Those attending patients are not known to have contracted the disease.

Pathology. There is a marked diffuse disturbance of the peripheral circulation with stasis, hemorrhage and transudation occurring primarily in the capillaries, which show endothelial destruction. The hemorrhagic tendency is said to be characteristic for certain organs--such as the outer medulla and surface of the cortex in the kidneys, subcapsular surface of the liver, the right atrium of the heart, the zona fasciculata of the adrenal cortex and the ciliary body of the eye. Albumenoid degeneration of the parenchyma occurs, particularly of the kidney, which also shows glomerulitis. Subarachnoid hemorrhage is occasionally seen.

Clinical course. Incubation period is 3-30 days, more commonly 14-21 days. There is no eschar. Onset is sudden with tremors, chills, fever, severe frontal headache, anorexia, nausea and vomiting. Prodromata may include fatigue, anorexia, malaise and myalgia for 1-7 days. Temperature rises to a peak of 104 - 105 F. by the 3rd day, then falls to normal or below by the 5th-6th day. This defervescence has no relationship to the prognosis, for the serious manifestations of the disease occur 1-2 days after the temperature falls. A petechial rash appears about the 3rd day, involving neck, axillary folds, arms and thorax. The rash has been described as morbilliform, individual lesions 1-2 mm. in size, frequently in the form of linear striations rather than of a petechial or macular rash, and is most often slight in extent, although it may become more widespread

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and severe as the disease progresses. Associated with this eruption there is a generalized flush about the face and neck. Mucosal and conjunctival hemorrhages nearly always occur along with severe injection of the corneal vessels. There is periorbital redness extending over the cheekbones. There is no perioral blanching and rarely herpetiform rash. Dermographism is present, and a slight edema of the face results in a characteristic vapid or stupid expression. Headache, nausea, vomiting, thirst, muscle and joint pains, insomnia and signs of cerebral damage may occur throughout the course of the disease, but usually increase in severity after defervescence. Paroxysms of hiccoughing and temporary myopia frequently occur. Pulse is relatively slow, but in serious cases, tachycardia develops. Blood pressure drops just before and after the temperature starts to decline. In severe cases the radial pulse may be almost imperceptible. There is very little diaphoresis. Even though pharyngeal inflammation is absent, painful deglutition is common. In more severe cases, hemoptysis, hematemesis, hematuria and melena may appear. No organ escapes the hemorrhagic diathesis. Renal involvement may cause anuria.

Under favorable circumstances, there is gradual recovery in about 2 weeks after onset, without sequelae. In some cases there may be cyclic recurrences of low-grade fever and slight hemorrhagic tendencies.

Laboratory. Urine - Albuminuria begins about the 3d day. Oliguria during defervescence may progress to anuria. Specific gravity is low and chlorides reduced. Microscopic to gross hematuria is usual.

Blood - Slight early rise in RBC falls with hemorrhagic diathesis, paralleled by Hb. Nucleated erythrocytes appear. There may be an early leukopenia followed by a true leukemoid leukocytosis sometimes reaching 80,000 per cu. mm. There is a shift to the left. Large plasma cells increase remarkably. Thrombocytes reach a low of 16,000-40,000 per cu. mm. by the 4th-5th day. Eosinophiles are present throughout the course.

Serology - Weil-Felix usually negative. Some patients show a weakly positive Wasserman.

CSF - Usually remains clear with normal pressure, but may show xanthochromia and pressure may rise to 200-300 mm.

Diagnosis. EHF should be considered in any individual in an established or suspected endemic area presenting acute onset of chills, fever, anorexia and vomiting associated with subsequent petechial rash about the neck, chest, upper arms and axillary folds. Subconjunctival and corneal injection, hemorrhage, hiccoughs, albuminuria, and leukemoid leukocytosis in the presence of eosinophiles and nucleated erythrocytes would further lead to this diagnosis. The dissociation between the febrile peak and the most serious period of the disease is also characteristic as is the later development of hemoptysis, hematemesis, hematuria and melena.

Prognosis. In general the prognosis is poor if there is bradycardia and hypotension at the 3rd day. Persistent hiccoughing is also a bad prognostic sign. Pulmonary hemorrhage or severe cerebral symptoms nearly always have a fatal termination. The case fatality rate averages 13.2% . (From a report by Ralph M.Takami, Captain, Medical Corps, U.S. Army, Medical Intelligence and

Epidemiology Officer, GHQFEC, dated 13 August 1951)

Control. Control of mites may be accomplished by elimination of the rodent hosts from the area to be inhabited by troops. Underbrush, vines and bushes should be cleared and all debris burned or removed. Vegetation and surface dirt may be scraped off with bulldozers. Area treatments with residual miticides are also effective. A 0.4 percent lindane spray applied to ground litter and low vegetation at the rate of 10-20 gallons per acre is recommended. A 10 percent emulsion concentrate, GSSO Stock #51-L-167-133 will soon be available for use by qualified personnel. This concentrate should be diluted 1-25. Protection of personnel in the field will require use of repellents. The current standard items, dimethyl phthalate, Stock No. 51-D-237-400 (2 oz. bottle) for personal use, and 51-D-237-425(1gal.) for treatment of clothing, are effective but will soon be replaced by newly developed items which will provide protection for much longer periods.

Note: This disease has been encountered by U. S. Forces in Korea. If suspected, the services of a virological diagnostic team should be requested, as further studies are needed. (Preventive Med. Div., BuMed.)

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What is Chronic Brucellosis?

A follow-up study of over 100 patients having brucellosis has revealed that a significant number of individuals complained of ill health one year after the onset of their illness. Many of these patients were considered as having chronic brucellosis. The basis for their state of ill health can be discussed under three categories. First, there was the group with a relapsing, febrile type of illness. There was no doubt that these individuals were ill from an objective point of view. The nature of the illness was amplified by a high titer of brucella agglutinins and, occasionally, by isolating brucella from the tissues and body fluids. Second, there was a group with evidence of localization of the disease in various organs and tissues of the body. In addition, serologic and bacteriologic studies defined the cause of the continued disability. Third, while little controversy would arise out of the foregoing two groups of patients with chronic brucellosis the problem of chronic brucellosis centers upon those patients who complain of poor health but in whom objective evidence of active disease cannot be demonstrated. This group comprised about 20 percent of all of the patients with brucellosis, including those who had received treatment with antibiotics. With almost monotonous regularity they complained of weakness, vague aches and pains, easy fatigability, nervousness and mental depression. With few exceptions, the titer of brucella agglutinins had declined and cultures remained sterile.

If the basic cause for the continued state of ill health in this third group of patients could be determined, the diagnostic problem of chronic brucellosis would be largely resolved. There appear to be three possible explanations for the complaints of this group. First, the symptoms are due to a continued active infection by brucella. Second, the complaints expressed by this group of patients

are not specific, and the symptoms fit in with the definition of the functionally disturbed psychoneurotic or neurasthenic patient. In the present study, the majority of the patients having prolonged illness without objective evidence of disease were emotionally unstable individuals. It may be postulated that these persons are suffering from the residuals of brucellosis, and that active disease is not present. Acute brucellosis does have an impact upon the nervous system, including the autonomic nervous system, and this impact may be reflected in a reaction pattern that persists long after the infection has subsided. Spink's observations indicate that patients bordering on a personality disorder or emotional disturbance may be tipped over into a functional state of chronic ill health by an attack of acute brucellosis. Furthermore, individuals with functional complaints or personality difficulties may have an exaggeration of these manifestations following acute brucellosis. Third, Apter and his associates have studied with psychometric tests a small group of patients having chronic brucellosis, and have suggested that the behavior patterns may be due to organic damage to the cerebral cortex. This possibility should be explored further.

Diagnosis. Studies in the author's clinic on the epidemiology and the natural history of brucellosis have demonstrated that certain basic requirements are necessary for a precise diagnosis of brucellosis; these include: (1) history of exposure to the disease; (2) objective as well as subjective evidence of illness; (3) the presence of brucella agglutinins, especially in a titer of 1 to 100 and above; (4) isolation of brucella from the tissues or body fluids. This often clinches the diagnosis, although the first three criteria may establish it with reasonable accuracy.

One is on very uncertain ground if the diagnosis is based upon: (1) subjective complaints only; (2) a positive intradermal test with brucella antigen; (3) absent, or low titer of brucella agglutinins. (Ann. Int. Med., Aug. 1951, W. W. Spink)

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Carcinoma of the Lung: Duration of Life of Individuals Not Treated Surgically

The widespread belief that individuals with untreated primary carcinoma of the lung seldom live longer than 2 years is used by many as a deciding factor in differential diagnosis, disease of longer duration being presumed nonmalignant. Current views respecting the comparatively short life of individuals with bronchiogenic carcinoma stem largely from observations of thoracic surgeons of patients whose disease for one reason or another cannot be treated surgically. But inasmuch as patients not subjected to operation are more apt to have advanced disease, this group cannot be used as a gauge of the average survival of all patients with bronchiogenic carcinoma. For the same reason the duration of life of nonoperated patients cannot be used as a yardstick of the results of resectional surgery.

This study was undertaken in the hope of obtaining additional information on a subject which is becoming increasingly important as more individuals are being discovered with bronchiogenic carcinoma and greater numbers subjected to surgery. Montefiore Hospital, New York City, where this study was made, admits patients with chronic diseases usually in advanced stages and the period of waiting to the wards is often long. As a result, a variable number of individuals with acutely progressive disease succumb either at home or in general hospitals before they have an opportunity to enter this institution. In evaluating the results of this study, this factor should be taken into consideration.

Study of 443 individual case records, including detailed autopsy protocols of 330, left certain impressions on the writers which cannot be translated into statistical forms. They believe that in the vast majority of individuals with bronchiogenic carcinoma, certainly the anaplastic form, lung resection is not the answer, however soon the the condition is diagnosed and treated. In fact, the earlier the operation the more problematic the outcome for the reason that generalization may have already taken the disease beyond the range of local measures. On the other hand, if symptoms have been present for 6 months to a year and there are still no signs of metastases, resectional surgery has more to offer. By the same token, the mere fact that the carcinoma may have been present for several years does not per se preclude a surgical attempt at removal, providing there are no signs of regional invasion. If the disease is a relatively slow-growing epidermoid carcinoma, especially if it originates in a peripheral bronchus, even better results may be expected. In spite of the dismal prognosis attending rapidly metastasizing bronchiogenic carcinomas every effort should be made to detect and treat the disease early in order to salvage as many individuals as possible in whom the carcinoma may fortunately be of a less virulent type. Early diagnosis will necessitate in many patients exploratory thoracotomy to supplement roentgenography, bronchoscopy and other diagnostic measures.

Any clinical bearing which this study may have on the treatment of bronchiogenic carcinoma will be better appreciated by comparing the natural span of life of such individuals with those submitted to operation. Strictly speaking, the 2 groups are not comparable. The surgical group had had symptoms for some time prior to operation and their survival time is traced to the time of operation; the length of life of nonsurgically treated patients is traced to the onset of symptoms. However, this discrepancy is partly offset by the fact that patients with inoperable carcinoma are more apt to be in advanced stages of their disease. With due allowance for the many variables, a comparison of the 2 groups is not beyond the province of this discussion.

In a collected series of 7,815 patients with bronchiogenic carcinoma, reported from 10 medical centers of the United States and England, probably repsenting the best obtainable with surgical treatment of bronchiogenic carcinoma, approximately one-third (2,490) were considered operable. In one-half of these (1,239), the tumor was found resectable and in the remaining half (1,251) nonresectable. Of the resectable group, 72 or 5.8 percent lived 5 years or longer. The 5 year survivals constitute less than 1 percent of the original group of patients. In contrast, of the 443 patients who died a natural death at the Montefiore

Hospital, 8 or almost 2 percent, lived 5 years or longer.

As is well known, statistics if not properly evaluated are apt to be misleading and this applies to the present series of cases no less than to some reported from other clinics. It should not be construed that an individual with bronchiogenic carcinoma has a better chance for survival if he is left alone. On the contrary, pneumonectomy in selected cases offers a much better prospect of longer living. These findings do suggest that operations on patients with advanced bronchiogenic carcinoma, as applies to most instances at present, are of no avail. In view of the high operative mortality rate (22 percent in the collected series), reduced in recent years, there is every reason not to subject an individual to operation unless there is reasonable expectation that the patient will stand the ordeal and obtain arrest of the disease. Too many individuals with bronchiogenic carcinoma are being subjected to operation on the supposition that death is a matter of months, and "nothing is lost by the attempt." The fact that 15 percent of a group of patients with bronchiogenic carcinoma lived 2 years and longer without surgery is food for thought. (Dis. of Chest., Sept. 1951, A. Buchberg, R. Lubliner & E H. Rubin)

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Carcinoid Tumors of the Gastrointestinal Tract

Carcinoid tumors were so designated by Oberndorfer in 1909 in the belief that they were actually benign lesions with histologic resemblances to carcinomas. They have also been known as argentaffinomas in deference to their affinity for the silver stains. It has been suggested that they be regarded as Grade 1 carcinomas, particularly when they involve the small intestine.

Carcinoid tumors are relatively uncommon. Dockerty and Ashburn estimated on the basis of an analysis of the material at the Mayo Clinic that carcinoid tumors of the ileum accounted for 23 percent of all malignant neoplasms affecting the small bowel. Malignant tumors of the small intestine constitute only 0.5 percent of all malignant neoplasms of the gastrointestinal tract.

These tumors originate in the chromargentaffin cells situated in the crypts of Lieberkühn. The segmental distribution of carcinoid tumors along the gastrointestinal tract varies in proportion to the number of these particular cells found in a given area. They occur most frequently in the appendix and then appear with decreasing frequency in the terminal ileum, jejunum, rectum, colon, cecum, stomach, gallbladder and duodenum.

A search of the files of the Lahey Clinic reveal that 31 carcinoid tumors have been observed in the period from 1931 to January, 1948. These neoplasms affected the various segments of the gastrointestinal tract in the following order of frequency: stomach, 1; colon, 1; ampulla of Vater, 1; ileum, 12 and appendix, 16. Thus, 50 percent of these tumors occurred in the appendix and 89 percent were confined to the region of the appendix and ileum.

Pathology. Masson has localized the origin of these tumors to proliferation of the Kultschitzky cell situated in the crypts of Lieberkühn. Dockerty and Ashburn in their analysis of carcinoid tumors of the ileum substantiate this theory. The specific physiologic function of these cells has not been precisely determined, although Best and Taylor related that various investigators have imputed an endocrine or enzymatic activity to them.

Grossly these tumors occur as solitary nodules in the appendix, but are frequently multiple when they are located in the ileum. It is largely agreed that these are multiple primary growths rather than metastatic manifestations. The primary tumor is usually small and not infrequently the metastatic lesions attain greater size than the original neoplasm.

These tumors, which are yellow or light orange in color, may occur at any point on the circumference of the bowel but are frequently antimesenteric in location. They are essentially submucosal in origin; but as they spread by centrifugal expansion, they invade the muscularis and mucosa and ultimately break through the serosa. They ulcerate more slowly than other varieties of gastrointestinal neoplasms and encroach on the lumen of the bowel secondarily. These particular features account for the infrequency of hemorrhage and the insidiousness of obstructive manifestations associated with these tumors.

Carcinoid tumors spread by direct extension through the submucosa, muscularis and serosa and by way of lymphatic channels and perineural spaces to regional lymph nodes. As the multiple lesions of the terminal ileum extend through the serosa and spread to involve conglomerate lymph nodes, loops of intestine become matted together and kinked, thereby producing obstructive symptoms.

Tumor-spread by blood vessel invasion was particularly evident in the case reported by Ritchie and Stafford, showing metastasis to the spleen, uterus and both ovaries with microscopic clusters of cells within vascular lumens. Liver metastases, which are generally indicative of spread by blood vessel involvement, occur with relative frequency in the presence of carcinoids of the small intestine.

Dockerty and Ashburn insisted that all carcinoid neoplasms are indeed malignant and it is well to designate them as Grade 1 adenocarcinomas (carcinoids) to suggest at once that they are universally malignant and of specific cell origin. Carcinoid tumors are composed of small cuboidal cells with small, deeply staining nuclei. The cells grow in groups and invade lymphatic channels and stream along nerve sheaths. They contain granules which have an affinity for certain silver stains. Mitoses are rarely seen.

Clinical Features. In the 31 cases observed at the clinic the youngest patient was 20 years of age and the oldest 69; the average age was 46.3 years. There were 10 males (32 percent) and 21 females (68 percent). Six of the tumors involving the ileum, 12 in the appendix and 1 in the colon were incidental findings at autopsy or were removed incidentally in a surgical specimen resected for another variety of primary lesion. In the 12 remaining cases the lesion was provocative of symptoms. These lesions were distributed as follows: 1 in the

stomach, 1 in the ampulla of Vater, 4 in the appendix and 6 in the ileum.

It should be remarked that of the 19 instances of asymptomatic carcinoid tumors studied 10 were associated with other malignant neoplasms. The associated diseases in the remaining 9 cases included cholecystic disease in 4 instances, fibroid uterus in 3 cases, adrenal tuberculosis in 1 case and retroverted uterus in 1 case. (Am. J. Surg., Sept. 1951, K. W. Warren & Capt. E. B. Coyle, MC, USN)

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Terramycin in the Treatment of Trachoma

On the basis of a study of treatment with terramycin in about 700 cases of trachoma the following conclusions are reached:

Early trachoma of less than 2 months' duration will respond promptly and well to terramycin without exception. A 0.1 percent terramycin hydrochloride ointment, as well as a 0.5 percent solution of the drug applied more than 4 times a day, will produce a clinical cure in the course of a few weeks. Too early discontinuation of treatment, however, is often followed by an inflammatory relapse. Treatment for 2 weeks after a clinical cure will be satisfactory for a permanent cure.

Chronic trachoma of several years' duration will respond fairly well to terramycin, but the best dosage of terramycin cannot be determined for all cases. A 0.5 percent ointment applied 3 times a day for 4 weeks, however, will be followed by cure in about 80 percent of cases, occurring during a 1-to-2 month follow-up period after the completion of treatment. A combination of surgical and terramycin therapy will give far better results. In cases in which the first course of treatments fails to cure, a second course of treatments is to be given, with an increased dose of terramycin or with surgical therapy combined with topical use of the drug. A third course of treatment will not be required in more than 5 percent of cases.

Acute pannus and ulceration of the cornea will uniformly respond promptly to terramycin treatment. Application of a small dose will produce a cure within several days. In pannus crassus, however, 2 weeks' treatment will be required before healing is complete, even with an increased dose.

In all these conditions, systemic administration alone seems to have little advantage over topical application. An ointment seems to be slightly more effective than a solution.

Since this paper was submitted for publication, the following results have been obtained:

1. During a 9 month period, among the patients with chronic trachoma cured by the first course of treatment, an actual relapse was observed in only 4 of the 243 patients examined.

2. A combination of terramycin ointment (0.5 or 1.0 percent, applied 3 times a day for 6 to 10 weeks) and sulfadiazine (1.5 Gm. daily given by the oral route for the first 10 days) resulted in cure in 15 of the 15 patients with chronic trachoma treated.

3. A terramycin (0.5 percent)-hyaluronidase (1 turbidity-reducing unit [TRU] per gram) ointment applied 3 times a day for 6 to 8 weeks resulted in cure in 10 of the 11 patients with chronic trachoma treated. (AMA Arch. Ophthal., Sept. 1951, Y. Mitsui, C. Tanaka, H. Toya, Y. Iwashige & K. Yamashita)

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A Recent Advance in Estrogenic Therapy

Whatever therapy is used, treatment in the menopause should be ultimately aimed at the avoidance of addiction. Naturally occurring estrogens have a significant advantage over all other preparations used for the alleviation of menopausal symptoms, in unusual control of the distressing disturbances and in general tonic effects. Since numerous controlled studies have repeatedly demonstrated that estrogenic substances orally administered are active, easy to administer, clinically effective and well tolerated by the patient, there is no need for parenteral administration.

A study was undertaken to investigate the effects of a newly prepared form of a naturally occurring estrogenic substance, piperazine estrone sulfate (Sulestrex), in reference to subjective relief and response of the vaginal epithelium. Twenty-five patients with various symptoms of the menopause, both of the natural and artificial type, were followed.

In 24 women, this medication gave complete relief on dosages varying from 1.5 mg. to 6.0 mg. daily. Cyclic therapy was initiated when control of the symptoms was obtained. Maintenance dosage varied from 0.75 mg. to 3.0 mg. daily.

No symptoms of intolerance to the drug were encountered, regardless of dosage. The annoying urinary taste and odor sometimes found in natural conjugated estrogen were not present. Withdrawal bleeding, the chief untoward effect of estrogenic administration, was noted in 1 patient, but was of such nature as not to require discontinuance of the medication.

Piperazine estrone sulfate evoked moderate epithelial cornification of the vaginal mucosa. The subjective improvement closely paralleled the change in cornification. It is concluded that piperazine estrone sulfate is an extremely useful estrogenic substance and is indicated wherever oral administration is preferred. (Am. J. Obstet. & Gynec., August 1951, W. J. Reich, M. J. Nechtow, A. M. Kurzon & M. W. Rubenstein)

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The Comparative Value of Amoebicidal Drugs

The large number of drugs at present in use for the treatment of amebic dysentery provides evidence of the doubts held by the medical profession about their individual efficacy. The shortcomings, as well as the efficacy of these drugs is well known. Part of the conflict in the literature about their therapeutic

value is due, at least in part, to the varied manifestations of amebiasis, which may range from a simple and symptomless infestation to a florid or even fulminating ulcerative colitis, with blood, mucus and amebic trophozoites in the stools.

During the past 5 years the authors have observed each year over 2,500 cases of acute ulcerative amebiases in African patients. The severity of the disease in the African, with his low nutritional status, may cause it to be more resistant to treatment. Because of the homogeneous nature of this vast number of cases, reasonably valid conclusions can be drawn concerning the comparative value of drugs. Accordingly, a series of therapeutic trials was started, in order to establish the value of the various amebicidal agents and to compare them with one another.

Method. Hundreds of cases were treated in a short period of time. Most of the series treated with an experimental drug comprised approximately 50 cases. Where there was a high failure rate in the early cases, statistical analysis was then made, and if it did not appear that the substance under trial was likely to fall in the competitive zone, no further cases were admitted to that series. Consequently, some series do not contain 50 cases.

All patients accepted for the trials series were complaining of diarrhea with blood and mucus, showed ulceration at sigmoidoscopy and had actively motile amebae in stools or ulcer scrapings. No patient passing cysts only was accepted in any of the series. Patients were also not included if they showed chloride deficiency, abdominal distension, sloughs on sigmoidoscopy or other signs which have been found to presage perforation or ileus, because it was thought unjustifiable to experiment on such severely ill patients. The cases accepted in this series represent a relatively uniform population, from which valid conclusions can be drawn by comparing the statistical results in the different series.

Sigmoidoscopy was performed before treatment and repeated at intervals. Ulcer scrapings were examined by the direct method; stools were subjected to zinc sulfate flotation in addition. Throughout all the series, an assessment of "immediate cure" was made at 20 days, and the percentages of successes and failures on this date is the basis of comparison. Results were classified into 3 categories: (1) success, i.e., symptom free, all ulcers healed and no amebae found in stools; (2) possible failure, i.e., usually symptom free, one or more ulcers still open but amebae not found in stools or scraping; (3) absolute failure, i.e., open ulcers still present and motile amebae still demonstrable.

Because at the onset of this work even the efficacy of the recognized amebicides was unknown, the known amebicides were tested separately, but when later experience indicated that certain additional therapies were likely to succeed, the authors felt that they could no longer risk the lives of patients who were obviously deteriorating. These cases were removed from the series and given additional drugs. From a statistical point of view, those cases which had 5 days, or more, of a test therapy were regarded as failures, but those with less than 5 days on a drug were discarded as unsuitable cases.

Emetine. Each patient in this series was given 1 gr. of emetine intramuscularly for 15 days. As emetine has been the most widely used drug in

amebic dysentery, this series has been considered a yardstick by which the effects of other drugs may be judged. Absolute failures numbered 28 percent and successes 50 percent. This series was investigated in 1947. In 1951 the results were checked by testing a further 18 cases with the same dose of emetine. Absolute failures numbered 27 percent and successes 55 percent. These results suggest the uniformity of the authors' cases and methods.

Diodoquin. Three tablets, each 0.21 Gm. were given 3 times daily for 20 days. Statistical analysis shows no significant difference between the effects of this drug and emetine.

Emetine Bismuth Iodide. There were 2 series tested with this drug. The dosage in each was the same, 3 gr. nightly for 10 nights. The first series was treated with commercial E. B. I. pills. Some of these were merely compressed; others were compressed and covered with a tenuous film of gelatine. Through the sigmoidoscope several pills of both kinds were recovered intact and not disintegrated. Radiographs of some of these patients during the course of treatment showed shadows of intact tablets in the lumen of the bowel. The results of treatment in this series were extremely unsatisfactory. That E. B. I. pills do not always disintegrate is known, but too often forgotten, particularly by the manufacturers. The authors had refused to use enteric-coated E. B. I. pills but had been lulled into a false sense of security by the appearance of the bare pills which suggested that they would readily break up. Since it was felt that this series was an unfair trial of E. B. I., a further trial was started with the same tablets crushed and placed in plain gelatine capsules. This reduced the absolute failure rate from 47 percent to 20 percent and raised the success rate from 40 percent to 56 percent. When given under the best conditions, the effect of E. B. I. shows no statistical difference from that of emetine.

Carbarsone. This drug was given in 4 gr. doses twice daily for 10 days. The absolute failure rate of 46 percent was significantly higher than the 28 percent with emetine. The success rate for carbarsone of 46 percent was not significantly different from the 50 percent for emetine.

Yatren (Chiniofon). This was given in doses of 0.5 Gm. 3 times daily for 3 days and then 1.0 Gm. 3 times daily for 7 days. The success rate showed a significant improvement on that for emetine. The failure rate was not significantly different from that for emetine. The authors conclude that chiniofon is of approximately equal value to emetine and ranks high on the list of amebicides. A disadvantage is the diarrhea which often follows its administration.

Milibis (Bismuth p-N-glycolylarsanilate). This new amebicide made by Winthrop was given in doses of 0.5 Gm. 3 times daily for 10 days. Since the authors found a high absolute failure rate of 62 percent and a low (24 percent) success rate, they decided that this drug compared so unfavorably with emetine that trial was abandoned after testing 20 cases.

Aralen (Chloroquine diphosphate). The dosage was 6 tablets (1.5 Gm.) on the first day, 4 tablets on the second day, and 2 tablets daily for 18 days. After treating 10 cases with a 50 percent failure rate and only 10 percent success rate, further trial was abandoned. By contrast, in the treatment of hepatic amebiasis, aralen has given good results.

P.76 and P.196. P.76 is phenyl di-iodo-hydroxy cinnamic acid. P.196 is ethyl di-iodo-hydroxy cinnamic acid. These products are both oxyquinoline derivatives submitted for trial by the Schering Corporation. Reference to one of these drugs, P.196 is made by Shlaes (1950) who reported moderate success. In the first P.76 series (14 cases), 1.2 Gm. and in the second (23 cases), 6 Gm. were given daily for 20 days. P.196 was given in doses of 3 Gm. daily for 20 days. The results of all 3 series were so bad that further experimentation was abandoned.

Control. The authors were asked officially to carry out trials on a widely advertised proprietary compound which subsequently proved to be inert. The results in 50 cases were so bad (absolute failure rate, 88 percent) that they may reasonably be accepted as a series of controls which received no treatment.

This investigation is unusual and of special interest because the cases have all conformed to a standard pattern of dysentery with visible ulceration and the presence of trophozoites, and because the authors were able to experiment with single drugs, thereby eliminating the difficulties of analysis inherent in comparing combined courses in which a single drug is varied. All the amebicides used, with the possible exception of P.196, have some genuine ameliorating effect; all were of some value. The object of the investigation was to seek evidence concerning the most and the least valuable.

The results refer only to what is termed "immediate cure." This involves considerably more than symptomatic relief, or even the disappearance of amebae and the healing of ulcers alone. Those patients only were accepted as successes in whom all visible ulcers were healed. It is realized that clearance of amebae and ulcers at the end of a short course of treatment is very different from permanent clearance and cure. On this latter subject, there is no information, because the patients refuse to return for follow-up. In any case, the patients would be a most unreliable source of information owing to the very serious risk of reinfection.

It is emphasized that this paper is purely a comparison of the effects of amebicidal drugs used singly and is not a recommendation for individual therapy. It has been shown elsewhere that some antibiotics, when used either alone or in combination with amebicidal agents, are far more efficacious. (J. Trop. Med. & Hygiene, Aug. 1951, A. J. Wilmot, T. G. Armstrong & R. Elsdon-Dew)

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The Prognosis of Portal Hypertension

Portal hypertension is believed to be due to some obstruction to the flow of portal venous blood within the liver or along the course of the portal or the splenic vein (Whipple 1945). The increased pressure gradient between the portal and systemic veins causes collateral vessels to open up at sites of actual or potential communication between the two systems. Of these sites the one of greatest clinical importance is the submucous plexus of venules at the lower end of the esophagus and the upper end of the stomach, where varicose dilatations may form. These varices may become eroded and cause severe gastrointestinal bleeding.

Gastrointestinal hemorrhage is the most dangerous complication of portal hypertension, and attempts have been made to reduce the risk of hematemesis by some form of portacaval anastomosis. If the results of these operations are to be adequately assessed, it is essential to know the prognosis of the syndrome when it is treated by more conservative measures. The survival of a consecutive series of patients with hemorrhage from demonstrable esophageal varice has therefore been studied.

Twelve patients had no clinical or biochemical evidence of liver damage, and the mortality in this group was nil. Thirteen of the 14 patients with liver damage have died during the period under review. Only 2 patients had portacaval anastomoses; the others were all treated by more conservative measures.

The prognosis of portal hypertension seems to be mainly determined by the state of liver function. In patients without clinical or biochemical evidence of liver damage, hemorrhage from varices is not so serious as it has sometimes been thought to be, especially when prompt and efficient blood transfusion is available, and the patients are young and otherwise fit. Furthermore, the hemorrhage is venous, and although the portal venous pressure is raised, it is still less than a third of the arterial pressure. The existence of liver damage alters the prognosis completely. The more severely the liver is damaged, the more dangerous is hematemesis likely to be, and in most of the patients dying under observation in hospital the immediate cause of death seemed to be hepatic coma. A hemorrhage insufficiently severe to cause death from acute blood-loss often precipitated coma from which the patient could not usually be roused even by adequate blood transfusion. Some of the patients developed the typical restless coma of acute hepatic failure, with irrational behavior and extensor plantar responses. Sometimes a patient died in coma 2 or 3 days after the last hemorrhage.

This is the background against which the results of portacaval anastomosis must be judged. Unfortunately patients with severe liver damage are poor operative risks and are usually considered unsuitable for radical surgery. At the other end of the scale, patients with no evidence of liver damage do so well on more conservative treatment that it is questionable whether operations with an appreciable mortality are justifiable. (The Lancet, Sept. 1, 1951, P. C. Reynell)

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The Surgical Treatment of Bleeding Intracranial Aneurysms

A series of 50 consecutive cases of leaking intracranial aneurysm was treated surgically by carotid ligation or an intracranial exposure, or by a combination of these procedures, with 9 deaths. Thirty-three patients made good recoveries; 5 patients, although disabled, are leading economically useful lives and 3 patients are severely disabled. These figures are compared with the mortality rate of between 50 and 60 percent and the satisfactory recovery rate of between 16 and 30 percent which follows conservative management in the ordinary run of cases of subarachnoid hemorrhage. Probably the mortality rate in the surgical series, had they not been submitted to operation, would have been higher than these figures.

It is felt that all cases of subarachnoid hemorrhage should be submitted as soon as possible to carotid arteriography, and that those cases in which an aneurysm or arteriovenous malformation is revealed should be operated on forthwith.

The treatment of choice for aneurysms of the intracranial internal carotid artery is felt to be stage-ligation of the common carotid artery, followed later by ligation of the internal carotid artery in the neck and by clipping of the intracranial internal carotid above the neck of the aneurysm and below the neck of Willis (i.e., trapping of the aneurysm).

The treatment of choice for aneurysms at the bifurcation of the internal carotid artery is a direct intracranial exposure and either wrapping the aneurysm with muscle or clipping its neck. This may be preceded by a preliminary carotid ligation.

The treatment of choice for aneurysms of the middle cerebral artery or of the proximal part of the anterior cerebral artery including the communicating artery is also by a direct intracranial exposure with wrapping of muscle around the aneurysm. Clipping the neck is sometimes efficacious, but carries the risk of operatively rupturing the aneurysm. These aneurysms are often associated with hemorrhage into the adjacent frontal or temporal lobes, and such intracerebral clots should be evacuated. In some cases a preliminary carotid ligation is required.

For aneurysms of the anterior cerebral artery distal to the communicating artery, trapping the aneurysm between clips or ligatures placed on the parent artery is felt to be a practical method. Carotid ligation is not required.

A single case of aneurysm of the posterior cerebral artery causing both subarachnoid hemorrhage and one isolated third nerve palsy is reported. It was treated by unilateral vertebral artery ligation.

It is felt that spontaneous subarachnoid hemorrhage is an emergency which calls for surgical handling. (J. Neurol., Neurosurg. & Psychiat., Aug. 1951, M. A. Falconer)

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Perforated Esophageal Ulcer

Various causes for esophagitis and esophageal ulcer have been considered: foci of infection, inadequate blood supply , ectopic gastric mucosa and regurgitation of gastric contents. Most authors now feel that repeated vomiting is the most important factor. Esophageal ulcer may be found at any age, but is most common in the 4th and 5th decades. Esophagitis and esophageal ulcer are frequently associated with hiatus hernia and duodenal ulcer, especially with obstructing duodenal ulcer. In a recent article, 60 cases of benign esophageal stricture associated with esophagitis were described. Of these, 34 also had hiatus hernia, 20 had duodenal ulcer and 16 had active esophageal ulcer.

Symptoms consist of pain, epigastric or substernal, radiating to the back and increasing during deglutition, vomiting, hematemesis, perforation, dysphagia, anemia, weakness and weight loss.

Hemorrhage is very frequent, possibly due to the vascularity of the lower end of the esophagus. Esophageal ulcer in a hiatus hernia has been incriminated as the cause of some cases of obscure anemia. Perforation is a not infrequent complication. The ulcer may perforate into the mediastinum or the abdomen, the latter being more common. Abdominal perforation gives the usual signs of ruptured hollow viscus. Perforation into the mediastinum gives a characteristic clinical picture. It often occurs during an attack of vomiting. There is sudden severe precordial or epigastric pain, associated with shock and dyspnea. The shock lasts for 2 to 3 hours, then the temperature rises and signs of pleural effusion develop. In 6 to 12 hours, subcutaneous emphysema may be noted in the neck. A roentgenogram of the chest may show any one or any combination of the following: air behind the heart, air in the upper mediastinum or a small pleural effusion. It is important to diagnose mediastinal perforation early since treatment by thoracotomy with drainage has proved successful in some cases.

An ulcer crater may be demonstrated on upper gastrointestinal series, but this is unusual. More commonly a spastic defect in the lower esophagus is found. Esophagoscopy is usually required for a definite diagnosis.

Most cases respond to the usual ulcer regime: progressive Sippy diet, aluminum hydroxide, tincture of belladonna and other medical measures. Healing may be very slow, some cases requiring 3 to 5 years.

Wangensteen has advocated gastrectomy for esophagitis to reduce the acidity and digestive capacity of the contents of the residual gastric pouch and quicken the gastric emptying time. He has had excellent results in intractable cases. (Am. J. Digest. Dis., September 1951, J. H. Coffey & I. Dravin)

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Occupational Cancer and Other Health Hazards in a Chromate Plant: A Medical Appraisal

This study consisted of a medical investigation of present and previous chromate workers as well as of 2 environmental groups. This latter category included office workers and workers of a cement plant, 1100 feet distant from the chromate plant, as well as workers exposed to chromium and chromium compounds in other occupations. A statistical random sample of workers was taken of the chromate plant population and a clinical study was conducted of this group through arrangements with the Cleveland Clinic. All the examinations were conducted by exceptionally well qualified physicians and the same procedures were carried out in each categorical test.

The observations made led to the following conclusions:

1. Workers exposed to the inhalation of chromate and chromite dust may develop various acute and chronic injuries to the tissues of the respiratory system, such as ulcers and perforations of the nasal septum, nasal mucosal

polyps, chronic rhinitis, acute and chronic sinusitis, mucosal polpys and hydrops of nasal sinuses, laryngitis, asthma, acute chemical pneumonitis, chromitotic pneumoconiosis and bronchiogenic carcinoma.

2. Similar, while usually less, severe and frequent reactions may be observed among persons employed in the immediate environment of chromate plants, such as office personnel and first aid workers.

3. Workers of a chromate factory seem to have an excessive liability to inflammatory and ulcerative conditions of the gastrointestinal tract caused by the ingestion of chromates.

4. Such workers exhibit, moreover, not infrequently a hyperleukocytosis or a leukopenia, a monocytosis and eosinophila, as well as a decrease in hemoglobin and, sometimes, an erythrocytotic reaction. The bleeding time is often lengthened.

5. Depending upon the intensity of exposure to chromium compounds, there exists in chromate workers as well as in environmental worker groups, a variable urine and blood chromium level. This persists for several years after cessation of exposure to chromium compounds, and thereby provides a relatively sensitive index of previous exposure.

6. Workers mainly exposed to chromate dust usually develop a higher blood chromium level than those having mainly contact with chromite dust.

7. The retention of chromium in the various tissues may account for the prolonged excretion of chromium with the urine and may also be related to the delayed cancerous effects observed in the lungs of former chromate workers. (Indust. Med. & Surg., Sept. 1951, T. F. Mancuso)

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A Clinical Study of the Anticoagulant Properties of Treburon

Treburon, a recently discovered polyhexuronic acid derivative, has properties similar to those of heparin. Treburon is the sodium salt of sulfated polygalacturonic acid methyl ester methyl glycoside. It has previously been reported by its experimental designation, Ro 2-3053. Preliminary investigation showed that Treburon has approximately one third of the anticoagulant potency of sodium heparin when administered intravenously in man. The dosage for intravenous therapy is, therefore, 3 times larger than that routinely used for sodium heparin. Further clinical experience with Treburon, particularly when administered intramuscularly, is reported.

Method. A modified Lee and White method was employed in which the coagulation time was determined in each of 2 tubes at room temperature (20-24°C.) instead of 37° C. The one stage prothrombin time test of Quick and a test to determine antithrombin activity (heparin assay-Quick) were also used. Treburon and sodium heparin produce an anticoagulant effect which can be measured by each of these tests. The coagulation time has been routinely used in hospitals to evaluate the heparin effect, because the test can be done at the bedside. This test, although it is acceptable for clinical work, does not measure

anticoagulant properties with any critical degree of accuracy. If heparin or a heparinoid substance is added to the blood, the reaction in the prothrombin test is delayed. Since the potency of heparin can be assayed by measuring its antithrombin activity, Quick's heparin assay method was used to measure the antithrombin activity in the blood after administration of Treburon or sodium heparin.

Treburon was given to a wide variety of patients with cardiovascular or other disease in order to investigate its anticoagulant properties and compare them with those of sodium heparin. One hundred and forty-two patients were used in this study; 80 received single intravenous injections, 13 received continuous intravenous drip injections, 37 received single intramuscular injections, 3 received repeated intramuscular injections, 5 received Treburon intramuscularly with dicumarol and 4 received Treburon orally.

Results. In an earlier study, the effects of Treburon and heparin in the same patients were reported. In this study, single intravenous doses as high as 500 mg. were given to 16 patients, administered in solution containing 50mg. of Treburon per cc. The coagulation time was greatly prolonged without producing any toxic or hemorrhagic complications. The Addis counts of 24 hour urine specimens were not significantly altered during or after administration of the drug.

From 600 to 800 mg. of Treburon was dissolved in 1,000 cc. of a 5 percent glucose solution and administered over a period of 3 1/2 to 5 3/4 hours, with good results. Administration of 500 cc. to 2 patients produced no effect.

Treburon is therapeutically effective when administered intramuscularly every 12 hours. The initial dose is usually 625 mg. Subsequent doses vary from 250 to 625 mg. It is possible to maintain the blood in a therapeutically satisfactory hypocoagulable state for 5 days or longer with intramuscular injections of Treburon given every 12 hours. When injections are spaced at this interval, there is seldom any accumulative effect of the drug. Treatment can be controlled by using the Lee and White coagulation time determination or the Quick one stage prothrombin time test. If the patient is given Treburon intramuscularly every 12 hours, it is necessary to determine the coagulation time before each injection during the first 36 hours in order to establish the proper dose for the patient. Subsequently, a daily coagulation time determination made before 1 of the 2 injections is given has been found satisfactory for practical purposes. The patients who were maintained on repeated intramuscular injections of Treburon for a period of 5 days received a total dose of approximately 3.5 Gm.

Five patients were given dicumarol at the same time they were given an initial dose of Treburon. The immediate anticoagulant effect was maintained with intravenous or intramuscular injections of Treburon until the dicumarol effect on prothrombin synthesis became effective (24 to 36 hours). At this time the Treburon injections were discontinued and dicumarol was given daily, according to the status of the prothrombin activity.

Six of 42 patients complained of a mild or moderate stinging pain at the site of the intramuscular injection of Treburon. The pain was never severe and seldom lasted more than 30 minutes.

It was found that Treburon is ineffective orally in doses as high as 2,000 mg.

No toxic reactions to the drug were observed during the course of this study. (Wisconsin M. J., Sept. 1951, J. S. Hirschboeck, F. W. Madison, J. J. Giliberti & A. V. Pisciotta)

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Blood Transfusions

The ease with which the clinician is now enabled to order and procure stored blood for transfusions has created a situation in which more transfusions are being given than is either wise or necessary. Many serious hazards continue to exist and blood transfusions are, both potentially and actually, a dangerous undertaking.

Many radical surgical procedures are entirely dependent upon the availability of very large amounts of blood at the time of operation. The result of this has frequently been to place demands upon the blood banks which could be met only by the use of blood which does not agree in Rh type with the Rh type of the patient.

If the patient is Rh negative and must receive Rh positive blood, the patient's serum must be tested for evidence of sensitization to the Rh factor, either by means of the Coombs test or the trypsinized red blood cell test. It is important that the test cells contain as many of the known blood factors as possible, since this broadens the spectrum of reactivity, i.e., permits the detection of a larger number of antibodies. Although the most frequent cause of isoimmunization is the D antigen, the other antigens of the CDE (viz., Rh positive) system are known to cause such immunization. The cde (viz., Rh negative) antigens have been known on rare occasions to produce immunization and subsequent hemolytic reactions.

Although these are problems which belong within the province of the blood bank and the hematologist, the surgeon and internist must be sufficiently acquainted with these facts so that they can understand the potential hazards involved. Approximately 50 percent of D negative individuals are sensitized by a transfusion of D positive blood. Between 50 and 75 percent of such individuals become sensitized "if the attempt at immunization is sufficiently prolonged." This is important, since many of the Rh negative patients who have received Rh positive blood at the time of operation will require further transfusions during the postoperative period or at some time thereafter. These patients may be difficult to type in the postoperative period, and may be incorrectly typed as Rh positive unless a careful check is maintained against a list of such patients.

The best procedure is to give these patients nothing but Rh negative blood after they have once received an Rh positive transfusion. In this way chances

of immunization are reduced. Furthermore, the chances of a hemolytic reaction due to an already existing but undetected immunization are avoided. The possibility of technical errors is also reduced by this rule. The patient's home physician should be notified that his Rh negative patient has received Rh positive blood so that any future transfusions will be given only after proper studies have been completed.

Obviously, no patient should receive blood of the wrong type if it can be avoided. There are occasions, however, when the demand must be balanced against the supply, and when it is not only justified, but necessary. If the patient is found to be sensitized to the Rh factor, there is no alternative except the use of Rh negative blood. In dire emergencies, even this rule must be discarded and the danger of a hemolytic reaction on the one hand weighed against death from hemorrhage or shock on the other.

There are at least 5 other hazards or disadvantages which make it mandatory for the clinician to weigh the advantages of transfusions against the dangers or inadvisability of giving blood. These are: (1) depression of erythropoeisis; (2) homologous serum jaundice; (3) artificial or iatrogenic polycythemia; (4) hemolytic transfusion reactions; (5) pyrogenic transfusion reactions.

During the postoperative period the patient may have a moderate reduction in circulating hemoglobin. During this phase it is frequently necessary to rely on intravenous rather than oral feeding. Blood is apparently not a rapidly utilized form of protein. A moderate depression in circulating hemoglobin may not be alleviated until the patient's nutritional status as a whole is corrected. There is further evidence that the artificial maintenance of a normal or near-normal level of hemoglobin acts as a depressant on erythropoeisis. Therefore, there is no rational basis for the use of blood solely for nutritional purposes, in the absence of a definite anemia.

The incidence of homologous serum jaundice continues to be distressingly high. This disease is transmitted by blood transfusions, as well as by plasma infusions and other means, such as contaminated syringes and needles. Every additional pint of blood increases the chances that the recipient will acquire this serious disease. The incidence of homologous serum jaundice from blood transfusions alone may be as high as 0.26 percent. Thus, in patients who receive 15 pints of blood, the incidence can be expected to be at least 2 percent. Mortality has been reported to be from 0.2 percent to 27 percent. Recovery from surgical procedures has often been retarded or prevented by the occurrence of hepatitis.

There have been occasional instances in which patients have been given an excess of blood and have as a consequence become polycythemic. It has been shown that such patients do not undergo anesthesia or surgical operations as well as those who are not plethoric. It is also well known that thrombotic episodes are common in polycythemia. The incidence of venous thrombosis, coronary thrombosis and even of cerebral and hepatic vein thrombosis can, therefore, be expected to be higher in those patients who have been transfused to the point of plethora.

It is, therefore, important to emphasize that plasma may be the agent of choice in some patients. Such patients include those with shock or bleeding, who require further expansion of the blood volume, but in whom the hematocrit is already elevated to or above normal levels. It is just as unwise to permit the hematocrit to rise above the range of 45 to 50 percent as it is to allow the continuation of severe anemia.

When one administers blood to a patient, he is to a certain degree dealing with unknown factors and unpredictable effects. Many pyrogenic and hemolytic reactions cannot be explained. Human errors, also, continue to exist in spite of the most rigid precautions. The incidence of hemolytic reactions is between 0.01 and 0.5 percent. The incidence of pyrogenic or urticarial reactions is usually between 1.8 and 2.7 percent. The mortality of hemolytic transfusion reactions has been reported to be approximately 50 percent. The mortality appears to be roughly proportional to the amount of blood given.

Failure to read carefully the labels on the bottles before giving blood to patients is probably the most frequent cause of hemolytic reactions. Another cause is improper labelling of the blood samples which are used for cross-matching. The best means of overcoming these errors is to insist that at least two people check both the name of the patient and the label on the bottle before the blood is administered.

For all of these reasons the clinician, and especially the surgeon, must give careful consideration to every transfusion which he orders. He must decide whether the loss by his patient of a few cubic centimeters of blood is sufficient cause for a transfusion. In postoperative periods he must decide whether or not a patient whose hemoglobin level is, for example, 12.0 Gm. per 100 cc. should be given a transfusion, or if more adequate general nutrition should be considered, or whether simple ferrous sulfate by mouth at a later date will suffice. He alone can decide whether or not to subject a patient to these risks, and he alone can decide that these risks are justified. (Surg., Gynec. & Obst., Oct. 1951, T. R. Talbot, Jr.)

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Further Studies of the Effects of Cortisone and ACTH on Neurological Disorders

Forty-five patients with various neurological disorders have been treated with cortisone or with ACTH. In 3 cases of myotonia dystrophica the myotonia was abolished during treatment with cortisone but it returned when treatment was discontinued. No improvement was noted in the dystrophic process. In 1 case of myotonia congenita the severe, generalized myotonia was abolished during treatment with ACTH. It returned, however, during treatment with DCA. The myotonia decreased again under treatment with cortisone.

Three cases of myasthenia gravis received cortisone. In 2 instances the myasthenia became much worse during treatment. Symptoms returned to their previous level when the hormone was stopped, but there was no rebound improvement. These observations may be of importance from the viewpoint of mechanism of the disease.

Three patients with dermatomyositis were improved by cortisone. The degree of improvement depends, however, upon the amount of fixed tissue damage. These cases are now regarded as medical emergencies.

A profound state of muscle dystrophy may occur during the course of acute disseminated lupus erythematosus. In 1 case this responded remarkably to cortisone. In another case the muscle weakness was unaffected by either ACTH or cortisone, although the constitutional symptoms such as fever were abolished.

Three cases of amyotrophic lateral sclerosis and 3 cases of peripheral motor neuropathy were uninfluenced by cortisone. Two cases of Raynaud's disease have been treated with cortisone. In 1 patient with induration and ulcer formation on the finger tips these skin changes cleared up. The other patient suffered from pure vasospasm and this was unaffected by the treatment.

Of 3 patients with polyarteritis, 2 were improved by cortisone. Relapse occurred when the drug was discontinued.

No improvement was noted in clinical symptoms of creatinuria in 3 cases of progressive muscular dystrophy of the childhood type. Seven of 8 cases of menopausal muscular dystrophy have shown striking improvement with cortisone, but maintenance dosage is necessary. (Brain, Sept. 1951, G. M. Shy & D. McEachern)

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Insecticidal Vaporizing Devices

The Interdepartmental Committee on Pest Control, composed of representatives of the Departments of Agriculture, Interior, and Defense, and the Federal Security Agency, has released (21 Sept. 1951) the following statement relative to the use of insecticidal vaporizing devices:

"It is the considered opinion of the Interdepartmental Committee on Pest Control that there are at present no data to indicate that the use of thermal generators dispensing only lindane, DDT, or mixtures of the two, for the control of flying insects is unsafe when the following restrictions are enforced:

1. The insecticide shall be released at the rate not to exceed 1 Gm. per 15,000 cubic feet per 24 hours.
2. Installation shall be made only in commercial or industrial premises, mess halls, and similar locations where human exposure will be on a working day basis - not continuous.

3. The devices should not be used in homes or sleeping quarters.

4. Devices shall be so constructed that output in excess of that recommended is impossible. Fuses to protect against overloading and high temperatures, and a pilot light to indicate whether or not the unit is operating should be 'built-in' features.

5. Units should be mounted above head height and 3 feet or more from the ceiling.

6. Installation shall be such that any material which might condense on nearby equipment, walls, or ceiling cannot be dislodged and fall into or otherwise contaminate food.

Since DDT and lindane are poisons, it is the opinion of the Committee that danger will arise from deliberate or unintentional violation of these basic principles."

This statement by the Interdepartmental Committee on Pest Control applies only to devices which are being promoted by several manufacturers for the control of flying insects within buildings. The devices are essentially wall brackets with built-in cups in which solid insecticide is vaporized by electrical heating elements. Field trials to determine the efficiency of these devices in comparison with other dispersal methods are currently underway. Procurement of these or other types of nonstandard equipment by naval activities is not recommended until results of these studies are available. Preliminary information indicates that continuous operation will be necessary for effective results, except in small spaces where intermittent operation may be adequate.

At present only lindane and/or DDT may be used in these vaporizing devices. Lindane appears to be the most readily vaporized in effective amounts. In some instances combinations with other substances which are themselves highly toxic or alter the safety factor have been proposed or sold. The concentration of insecticide in the air when released at the stipulated maximum rate does not become great enough to cause deposits on food or sufaces in the working area in significant amounts. However, over a period of time condensation close to the generator, particularly on the ceiling, may build up deposits of insecticide on the ceiling or walls which could flake off and contaminate food if it fell into preparation or serving areas. Item 6 provides a safety factor to cover this possibility.

It is a responsibility of cognizant Medical Department personnel to advise commanding officers that where insecticide vaporizing devices of this type are used, the restrictions listed by the Interdepartmental Committee on Pest Control must be strictly enforced. (Preventive Med. Div., BuMed)

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Medico-Military Symposium

A Medico-Military Symposium will be held at U. S. Naval Hospital, Chelsea, Massachusetts, 29 October - 3 November 1951. Interested personnel should contact Commanding Officer of Hospital.

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Course in Medical Aspects of Special Weapons and Radioactive Isotopes

The first course for the fiscal year 1952 in Medical Aspects of Special Weapons and Radioactive Isotopes is scheduled to convene at the U. S. Naval Medical School, Bethesda, Maryland, on Monday, 26 November 1951 and continue to 1 December 1951.

The course will present problems likely to be confronted and technics to be employed by medical and dental officers in the field of radioactivity. The subjects will be presented by speakers of outstanding prominence in their specialties; hence, the presentation will be interesting and informative to all Medical Department officers.

This course is conducted primarily for the benefit of inactive Reserve Medical Department officers; however, a limited number of officers of the Medical Department on active duty may be given "Authorization Orders" (no expense to the government) in accordance with paragraph 3 of BuPers-BuSandA joint letter of 16 March 1951. Inactive Reserve Medical, Dental, Medical Service Corps, and Nurse Corps officers residing in the 1st, 3rd, 4th, 5th, 6th, 8th, 9th Naval Districts and Potomac River Naval Command who desire to attend this course should submit their request for 6 days' training duty to the Commandant's office at the earliest practicable date. Meals and a limited number of sleeping quarters will be available. Quarters will be available on a "first come, first served" basis.

It is desired to invite inactive reserve personnel's attention to the fact that acceptance of orders to attend these courses WILL NOT, in any way, increase the possibility of involuntary recall to active duty of the personnel concerned. Therefore, inactive reserve Medical Department personnel are encouraged to take advantage of this opportunity to attend this course on active training duty orders in a pay status. (Reserve Div., BuMed)

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From the Note Book

1. The following exhibits were presented by the Bureau of Medicine and Surgery at the 58th Annual Convention, Association of Military Surgeons, October 8-10 1951, Chicago, Illinois: (1) New Methods of Preserving Skin, Bone and Blood Vessels; (2) Some Aspects of the Navy's Tuberculosis Control Program; (3) Post-traumatic Subcutaneous Granulomas, Associated with a Crystalline Material; (4) Blood and Blood Products in Atomic Warfare; (5) The Navy Nurse Corps, a Career in Nursing. (PIO BuMed, 26 Sept. 1951)

2. A Swiss discovery of a new insecticide, that knocks down and kills flies resistant to DDT was announced to the World Chemical Congress recently. The insecticide is called Pyrolan and the claim is that it is not dangerous to man and other warm-blooded animals. In Switzerland and Sardinia Pyrolan has freed, for several weeks, rooms of flies that were not affected by DDT. Moreover, the house fly does not seem to develop a resistance to Pyrolan. (Science News Letter, 22 Sept. 1951)

3. Successful use of an artificial heart and lungs to tide over circulation of blood in patients undergoing critical heart and general chest surgery can be expected in the near future, it was reported by Dr. John Gibbon at a symposium on artificial heart-lung machines at the National Institutes of Health. Scientists working with him have already been able to carry the circulation of dogs in their machine for as long as 127 minutes. (News release, NIH, PHS, FSA, 24 Sept. 1951)

4. Litter bearers and other members of medical teams in actual combat will be among the first to test new-type Army plastic and nylon armor against bullets and low-velocity shell fragments. The new jackets, helmets and suits should decrease the number of casualties among medical personnel and vehicle operators. (Military Notes, J.A.M.A., 22 Sept. 1951)

5. Fluoroscopy with gamma rays has been accomplished, and it may have useful applications. The compactness of the source and its freedom from reliance on power lines are important advantages. (Nucleonics, Sept. 1951, C. Garrett & A. Morrison)

6. Cure of a patient with a highly resistant strain of Streptococcus viridans endocarditis, treated with an average daily dose of 86 million units of penicillin for 28 days is reported. (Am. Heart J., Sept. 1951, R. L. Whipple, Jr.)

7. Functional malocclusion in orthodontics is discussed in the American Journal of Orthodontics, September 1951, by B. C. Madsen.

8. The changes in urine and serum electrolytes and plasma volumes after major intrathoracic operations is discussed in Journal of Thoracic Surgery, September 1951, by R. K. Finley, J. Y. Templeton, R. H. Holland and J. H. Gibbon.

9. The diagnosis and management of paralysis of the extrinsic ocular muscles with special reference to surgical treatment in 219 cases appears in British Journal of Ophthalmology, September 1951. (T. K. Lyle, A. G. Cross)

10. Thirty-two bed-ridden, aged patients with arteriosclerosis and mental confusion were treated orally with metrazol for a minimum of 90 days. The results obtained in this small series of cases indicate that metrazol is an effective and safe analeptic and of definite value in geriatric practice. (Geriatrics, Sept.-Oct. 1951, E. J. Chesrow, A. J. Giacobe, P. H. Wosika)

11. The clinical applications of cytologic diagnostic technics in the early diagnosis of primary lung cancer appears in Diseases of the Chest. (Sept. 1951, S. M. Farber, A. K. McGrath, Jr., M. A. Benioff & L. W. Espen)

12. A brief study with review of the medical history of the Russo-German war, 1941-1945 appears in the Military Surgeon, September 1951. (Lt. Col. C. F. Mayer, MC, USAR)

13. Acute erythroblastopenia in sickle-cell anemia and infectious mononucleosis is discussed in A. M. A. American Journal of Diseases of Children, A. I. Chernoff and A. M. Josephson.

14. A method for dissection and electrical study in vitro of mammalian central nervous tissue is described in Science, 21 Sept. 1951. (D. O. Rudin, G. Eisenman).

15. A critical review of the malformations of the eustachian tube, the middle ear and its appendages appears in A. M. A. Archives of Otolaryngology, Sept. 1951, F. Altmann.

16. The Bureau of Medicine and Surgery, on invitation of the Optometric Association of Alabama, displayed an exhibit entitled, "A Resume of Optometric Science in the U. S. Navy" from 1 October to 6 October 1951 at the Alabama State Fair Grounds. (PIO, BuMed, 3 Oct. 1951)

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BUMED CIRCULAR LETTER 51-131 26 September 1951

From: Chief, Bureau of Medicine and Surgery
To: All Ships and Stations Having Medical Department Personnel Attached

Subj: BUMED Circular Letter No. 51-125; modification of

1. Modify BUMED Circular Letter No. 51-125 as follows:

a. In paragraph 2b(2)(c), change column "C" to "D."

b. In paragraph 2b(4), change "columns A and B" to "column C."

H. L. Pugh

The above letter will not be printed in the Navy Department Bulletin.

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BUMED CIRCULAR LETTER 51-132 26 September 1951

From: Chief, Bureau of Medicine and Surgery
To: All Medical Department Activities and Facilities

Subj: Blood typing

1. The attention of all personnel of the Medical Department is directed to the necessity for constant vigilance in blood-typing procedures. The importance of accurate grouping is readily apparent under the present large-scale use of whole blood transfusions.

2. To achieve the required accuracy it is imperative that:

a. technicians are fully qualified;
b. accurate clerical procedures are followed;
c. approved techniques of typing are rigidly adhered to;
d. close supervision by a qualified medical officer be maintained

3. All activities performing blood typing are directed to survey their present procedures to the end that any possible source of error may be eliminated.

H. L. Pugh

The above letter will not be printed in the Navy Department Bulletin.

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BUMED CIRCULAR LETTER 51-133 28 September 1951

From: Chief, Bureau of Medicine and Surgery
To: All BuMed Managed Activities, Continental

Subj: Typewriters; purchase, utilization, replacement, and disposal

Ref: (a) BuMed Cir ltr 51-112 of 30 July 1951
(b) OMN ltr M71:KAG:ilh OGC/MHS:mbr serial 121 of 18 June 1951 and enclosure thereto
(c) NPR&D Reg. No. 1 (Revision of 15 Apr 1949)

1. Reference (a) is hereby cancelled and superseded.

2. By reference (b) this Bureau was assigned responsibility for enforcing at its management control activities the provisions of Personnel Property Management Regulation No. 18 of the General Services Administration.

3. Accordingly all activities shall immediately effect measures to insure:

(a) That all persons within the command are cognizant of and comply with instructions relative to adequate and proper care of typewriters.

(b) That repairs to typewriters are accomplished only by qualified personnel.

(c) That machines are distributed so that their maximum life is assured. (Reassignment of machines should be planned in order that those in the best mechanical condition will be available for the most exacting service and those in poorer condition will be assigned to less important operations.)

(d) That wide-carriage and special type machines used for limited periods of time should be so distributed to enable several departments to have access to them as required.

4. The following <u>minimum</u> standards for the replacement of typewriters have been established:

"Typewriters shall not be purchased for replacement purposes unless it is determined that the estimated cost of necessary repairs or rebuilding of each typewriter being replaced will equal or exceed at lowest available rates of the percentage of replacement costs as shown in the 'Standard Replacement Cost Percentage Scale'. Replacement cost as used herein is the current price of a replacement typewriter less the sale price or trade-in value of the used typewriter."

Standard Replacement Cost Percentage Scale

Percentage of replacement cost (new price less sale or trade-in value) which will justify replacement in lieu of repair----------	Year after year-of-manufacture as shown by manufacturer's serial number									
	2d	3d	4th	5th	6th	7th	8th	9th	10th	11th	12th
	80%	80%	80%	70%	70%	60%	50%	40%	30%	20%	10%

5. This directive shall not be interpreted to mean that replacement is mandatory when standards permit replacement. Equipment which is in useable and workable condition shall be retained and used even though standards permit replacement.

6. Activities submitting requisitions for typewriters shall indicate thereon the following information:

(a) The number of typewriters on hand.
(b) Whether the requirement is for replacement of typewriters or additional typewriters.
(c) If for replacement, the serial number, make, year, and estimated cost of reconditioning to place in first class condition, of each typewriter being replaced shall be included.
(d) Certification that present requirements cannot be filled from supply of typewriters on hand at the activity.

7. Excess machines shall be reported in accordance with reference (c).

8. Personal Property Management Regulation No. 18 defines "typewriter" as follows:

"'Typewriter' means manually and electrically operated machines, having standard or special keyboards, designed to produce printed characters by impression of type upon paper through the medium of an inked ribbon. It includes the varityper, hektowriter, proportional spacer and portable-type machines, but does not include bookkeeping, billing, or teletype machines."

C. J. Brown
Acting

The above letter will not be printed in the Navy Department Bulletin.

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Course in Aviation Medicine

The next class in Aviation Medicine will convene at the U. S. Naval School of Aviation Medicine, NAS, Pensacola, Florida, on 7 January 1952. The course consists of approximately 6 months of academic instruction in Aviation Medicine and flight indoctrination training, and leads to the designation of U. S. Naval Flight Surgeon.

The class will be limited to 30 students and is open to medical officers of the Regular Navy and Reserves of the rank of Lieutenant Commander and below. An agreement to remain on active duty for 1 year after completion of the course must be included with each application. Classes will be convened approximately every 3 months and those applications not accepted or those received too late for consideration for the 7 January 1952 class shall be held for possible enrollment in those classes convening later during the year.

Medical officers who wish to apply for the class convening 7 January 1952 should do so as soon as possible in order that their requests will reach the Bureau of Medicine and Surgery prior to 20 November 1951. (Aviation Med. Div., BuMed)

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NAVY DEPARTMENT
BUREAU OF MEDICINE AND SURGERY
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